

REMARKS

Favorable reconsideration of this application as presently amended respectfully requested.

RECEIVED
DEC 17 2001
TECH CENTER 16012900

Claims 1-3, 5, 7-12, 15-19, and 26-27 stand rejected under 35 U.S.C. 102(b) as being anticipated by Saros *et al.* (U.S. Patent No. 4,853,336) for reasons of record. This rejection is respectfully traversed with respect to the claims as amended.

Claim 1 as amended now claims a flow cytometry apparatus in which a portion of a fluid flow stream containing samples separated by a separation gas is contained within tube having an internal diameter of 0.02 inches or less when the fluid flow stream passes through a peristaltic pump. However, Saros *et al.* neither teaches nor suggests the unexpected advantages to be obtained by using a tube having an internal diameter of 0.02 inches or less in a flow cytometry apparatus. As noted in Larry Sklar's June 20, 2001 Declaration Under 37 C.F.R. § 1.132 (submitted with Applicants' June 21, 2001 Amendment) experiments conducted in his laboratory indicated "that integrity of bubbles used to separate samples is important for proper sample separation in the flow cytometry apparatus of the present invention" (See Sklar Declaration, paragraph 6) and "that the integrity of the bubbles used to separate samples in the flow cytometer is compromised when the inner diameter of the tubing is greater than 0.02 inches" (See Sklar Declaration, paragraph 7). As has been held by the Court of Appeals for the Federal Circuit, "[o]ne way for a patent applicant to rebut a prima facie case of obviousness is to make a showing of 'unexpected results,' *i.e.*, to show that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected." *In re Soni*, 34 USPQ2d 1684, 1687 (Fed. Cir. 1995).

Applicants have unexpectedly discovered that tubing having an inner diameter of 0.02 inches or less have the unexpected property of preserving the integrity of the bubbles, separation gas, used to separate samples in the flow cytometry apparatus of claim 1. Therefore, Applicants have shown that the claimed range of 0.02 inches or less achieves unexpected results relative to the teachings of the prior art. In fact, Saros *et al.* provides no teaching or suggestion with respect to the controlling the inner diameter of a tube used in a flow cytometry apparatus, much less teaching or

suggesting the advantages of claim 1's range. Also, contrary to what is stated in the Office Action, Applicants have not merely discovered an "optimum of workable ranges" (See Office Action, p. 8), but have in fact discovered that the claimed range provides substantially improved results, the standard set forth by the Federal Circuit in *In re Soni*, 34 USPQ2d 1684,1688 (Fed. Cir. 1995). Therefore, claim 1 as amended is patentable over Saros *et al.*

Claims 2-3, 5, 7, 9-12, 15-19, and 26-27 depend directly or indirectly from claim 1, and, accordingly, include all of the patentable features of claim 1 as well as other patentable features. Therefore, claims 2-3, 5, 7-12, 15-19, and 26-27 are patentable over Saros *et al.* for the reasons discussed above with respect to claim 1.

With respect to claim 8, the above rejection has been rendered moot by the cancellation of claim 8.

Based on paragraph 4 of the September 13, 2001 Office Action, claims 4, 6, 13-14, and 20-24 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Saros *et al.* in view of Kercso *et al.* (U.S. Patent No. 6,132,685) for the reasons of record (the March 28, 2001 Office Action). This rejection is respectfully traversed.

As discussed above, Saros *et al.* fails to teach or suggest claim 1's feature of a tube having an inner diameter of 0.02 inches or less. Kersco *et al.* is only cited for showing the use of "multiwell microtiter plates" and microfluidic channels "fabricated on [a] planar substrate comprising polymeric materials which are inherently hydrophobic such as polyvinylchloride (PVC) and polyurethane" as set forth in the March 28, 2001 Office Action at pp. 6-7, the "reasons of record" (The March 28, 2001 Office Action provides the "reasons of record" referred to in the rejection set forth paragraph 4 of the September 13, 2001 Office Action). Also, as noted in the March 28, 2001 Office Action, Saros *et al.* and Kersco *et al.* fail to disclose "an inner diameter of 0.02 inches (See March 28, 2001 Office Action, p. 7). Therefore, Kersco *et al.* does not remedy the deficiencies of Saros *et al.* with respect to failing to teach an inner diameter of 0.02 inches or less and claim 1 is patentable over the combination of Kersco *et al.* with Saros *et al.*

Claims 4, 6, 13-14, and 20-24 depend directly or indirectly from claim 1, and, accordingly, include all of the patentable features of claim 1 as well as other patentable features. Therefore, claims 4, 6, 13-14, and 20-24 are patentable over the

combination of Kersco *et al.* with Saros *et al.* for the reasons discussed above with respect to claim 1.

Based on paragraph 8 of the September 13, 2001 Office Action, claim 25 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Saros *et al.* in view of Kersco *et al.* and in further view of Farrell *et al.* (U.S. Patent No. 5,788,927) for the reasons of record (the March 28, 2001 Office Action). This rejection is respectfully traversed.

As discussed above, the combination of Kersco *et al.* and Saros *et al.* fails to teach or suggest claim 1's feature of a tube having an inner diameter of 0.02 inches or less. Farrell *et al.* is only cited for suggesting an inverted mounting design of a well plate (See March 28, 2001 Office Action, p. 11). Therefore, Farrell *et al.* does not remedy the deficiencies of the combination of Kersco *et al.* and Saros *et al.* with respect to failing to teach an inner diameter of 0.02 inches or less and claim 1 is patentable over the combination of Kersco *et al.* with Saros *et al.*

Claim 25 depends indirectly from claim 1, and, accordingly, include all of the patentable features of claim 1 as well as other patentable features. Therefore, claim 25 is patentable over the combination of Farrell *et al.* with Kersco *et al.* and Saros *et al.* for the reasons discussed above with respect to claim 1.

Based on paragraph 9 of the September 13, 2001 Office Action, claims 1-3, 8-12, 5-19, and 26-27 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Parce *et al.* (U.S. Patent No. 6,150,180) in view of Hach *et al.* or Trinel *et al.* (U.S. Patent No. 4,116,631) for the reasons of record (the March 28, 2001 Office Action). This rejection is respectfully traversed with respect to the claims as amended.

Claim 1 as amended now claims a flow cytometry apparatus in which a portion of a fluid flow stream containing samples separated by a separation gas is contained within tube having an internal diameter of 0.02 inches or less when the fluid flow stream passes through a peristaltic pump. However, Parce *et al.* neither teaches nor suggests the unexpected advantages to be obtained by using a tube having an internal diameter of 0.02 inches or less in a flow cytometry apparatus. As noted in Larry Sklar's June 20, 2001 Declaration Under 37 C.F.R. § 1.132 (submitted with Applicants' June 21, 2001 Amendment) experiments conducted in his laboratory indicated "that integrity of bubbles used to separate samples is important for proper

sample separation in the flow cytometry apparatus of the present invention” (See Sklar Declaration, paragraph 6) and “that the integrity of the bubbles used to separate samples in the flow cytometer is compromised when the inner diameter of the tubing is greater than 0.02 inches” (See Sklar Declaration, paragraph 7). As has been held by the Court of Appeals for the Federal Circuit, “[o]ne way for a patent applicant to rebut a prima facie case of obviousness is to make a showing of ‘unexpected results,’ *i.e.*, to show that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected.” *In re Soni*, 34 USPQ2d 1684, 1687 (Fed. Cir. 1995).

Applicants have unexpectedly discovered that tubing having an inner diameter of 0.02 inches or less have the unexpected property of preserving the integrity of the bubbles, separation gas, used to separate samples in the flow cytometry apparatus of claim 1. Therefore, Applicants have shown that the claimed range of 0.02 inches or less achieves unexpected results relative to the teachings of the prior art. In fact, *Parce et al.* provides no teaching or suggestion with respect to the controlling the inner diameter of a tube used in a flow cytometry apparatus, much less teaching or suggesting the advantages of claim 1’s range. In fact, because *Parce et al.* fails “to disclose a means for introducing a separation gas between each of the plurality of samples”, as admitted in the March 28, 2001 Office Action (see March 28, 2001 Office Action, p. 11), *Parce et al.* can teach nothing about using particular inner tube diameters to improve bubble integrity between samples. Also, contrary to what is stated in the Office Action, Applicants have not merely discovered an “optimum of workable ranges” (See September 13, 2001 Office Action, p. 8), but have in fact discovered that the claimed range provides substantially improved results, the standard set forth by the Federal Circuit in *In re Soni*, 34 USPQ2d 1684, 1688 (Fed. Cir. 1995). Therefore, claim 1 as amended is patentable over *Parce et al.*

Hach et al. is only cited for disclosing “a pump and a means for periodically injecting a separation gas (air bubbles) in the sample tubing to separate liquids and clean sweep the tubing” as set forth in the March 28, 2001 Office Action at p. 11, the “reasons of record” (The March 28, 2001 Office Action provides the “reasons of record” referred to in the rejection set forth paragraph 9 of the September 13, 2001 Office Action). Therefore, *Hach et al.* does not remedy the deficiencies of *Parce et al.* with respect to failing to teach an inner diameter of 0.02 inches or less and claim 1 is patentable over the combination of *Hach et al.* with *Parce et al.*

Trinel *et al.* is only cited for disclosing “an automatic flow analysis apparatus wherein samples are separated by intermediate segments of decontamination solution and wherein spacing between the samples and the decontamination solution are effected by segments of an separation inert gas [sic]” as set forth in the March 28, 2001 Office Action at p. 11, the “reasons of record” (The March 28, 2001 Office Action provides the “reasons of record” referred to in the rejection set forth paragraph 9 of the September 13, 2001 Office Action). Therefore, Trinel *et al.* does not remedy the deficiencies of Parce *et al.* with respect to failing to teach an inner diameter of 0.02 inches or less and claim 1 is patentable over the combination of Trinel *et al.* with Parce *et al.*

Claims 2-3, 9-12, 15-19, and 26-27 depend directly or indirectly from claim 1, and, accordingly, include all of the patentable features of claim 1 as well as other patentable features. Therefore, claims 2-3, 9-12, 15-19, and 26-27 are patentable over the combination of Hach *et al.* or Trinel *et al.* with Parce *et al.* for the reasons discussed above with respect to claim 1.

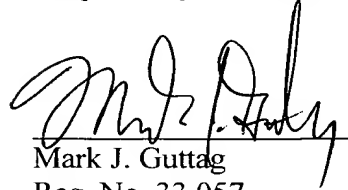
With respect to claim 8, the above rejection has been rendered moot by the cancellation of claim 8.

If the Examiner has any questions or concerns regarding the present response, the Examiner is invited to contact Mark J. Gutttag at 703-591-2664.

Serial Number: 09/501,643

In view of the foregoing, it is respectfully submitted that this application is now in condition for allowance, and favorable action is respectfully solicited.

Respectfully submitted,



Mark J. Gutttag
Reg. No. 33,057

JAGTIANI + GUTTAG
Democracy Square Business Center
10379-B Democracy Lane
Fairfax, Virginia 22030
(703) 591-2664

December 13, 2001

A circular stamp from the OIPE Patent & Trademark Office. The text "OIPE" is at the top, "PATENT & TRADEMARK OFFICE" is at the bottom, and "DEC 13 2001" is in the center. The code "JC185" is written to the right of the stamp.

)
)
)
)
) **Art Unit: 1641**
)
)
) **Examiner: GABEL. G**
)
)

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Please cancel claim 8 without prejudice or disclaimer.

- means for selectively analyzing each of said plurality of samples for said particles in a flow cytometer, wherein a portion of said fluid flow stream passing through said peristaltic pump is contained within tube having an internal diameter of 0.02 inches or less.

2. (Amended) The flow cytometry apparatus of claim 1, wherein said means for moving said plurality of samples further comprises an autosampler.

3. The flow cytometry apparatus of claim 2, wherein said autosampler includes a probe and said flow cytometry apparatus includes a means for exposing a probe tip of said probe to a jet of gas to remove liquid from said probe tip.

4. The flow cytometry apparatus of claim 2, wherein said autosampler includes a probe having a conical tip.

5. The flow cytometry apparatus of claim 2, wherein said autosampler includes a hydrophobic probe.

6. The flow cytometry apparatus of claim 5, wherein said probe comprises a hydrophobic material.

7. The flow cytometry apparatus of claim 5, wherein said probe is coated with a hydrophobic material.

9. (Amended) The flow cytometry apparatus of claim 8~~1~~, ~~wherein a portion of said fluid flow stream passing through said peristaltic pump is contained within wherein~~ said tube comprises a high speed multi-sample tube.

10. (Amended) The flow cytometry apparatus of claim 8~~1~~, wherein said peristaltic pump is located along said fluid flow stream between said autosampler and said means for selectively analyzing said plurality of samples.

11. The flow cytometry apparatus of claim 10, further comprising a single length of tubing extending from said autosampler to said means for selectively analyzing said plurality of samples.

12. (Amended) The flow cytometry apparatus of claim 11, wherein said single length of tubing comprises a high speed multi-sample tubing~~tube~~.

13. (Twice Amended) The flow cytometry apparatus of claim 121, wherein said high speed multi-sample ~~tubing-tube~~ comprises a poly vinyl chloride ~~tubetubing~~ having an inner diameter about 0.01 to about 0.03 inches and a wall thickness of about 0.01 to about 0.03 inches.

14. (Twice Amended) The flow cytometry apparatus of claim 121, wherein said high speed multi-sample ~~tubing-tube~~ comprises a poly vinyl chloride ~~tubing-tube~~ having an inner diameter about 0.02 inches and a wall thickness of about 0.02 inches.

15. The flow cytometry apparatus of claim 1, wherein said separation gas comprises air.

16. The flow cytometry apparatus of claim 1, wherein said plurality of samples are homogenous.

17. The flow cytometry apparatus of claim 1, wherein said plurality of samples are heterogeneous.

18. The flow cytometry apparatus of claim 1, wherein said particles comprise biomaterials.

19. The flow cytometry apparatus of claim 18, wherein said biomaterials are fluorescently tagged.

20. The flow cytometry apparatus of claim 1, further comprising a well plate including said plurality of respective source wells.

21. The flow cytometry apparatus of claim 20, wherein said well plate includes at least 96 source wells.

22. The flow cytometry apparatus of claim 20, wherein said well plate includes at least 384 source wells.

23. The flow cytometry apparatus of claim 20, wherein said well plate includes at least 1536 source wells.
24. The flow cytometry apparatus of claim 20, wherein said well plate includes wells having a conical shape.
25. The flow cytometry apparatus of claim 20, wherein said well plate is mounted in an inverted position.
26. The flow cytometry apparatus of claim 1, further comprising a means for injecting a buffer fluid between adjacent samples in said fluid flow stream.
27. The flow cytometry apparatus of claim 1, wherein at least one of said plurality of samples includes a drug present therein.